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| 09/743,107 | 08/21/2001 | Lars A. Hanson | 003300-723 | 5780 |

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| EXAMINER | |
|---|---|
| KAM, CHIH MIN | |
| ART UNIT | PAPER NUMBER |
| 1656 | |

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/743,107 | HANSON ET AL. | |
| | Examiner | Art Unit | |
| | Chih-Min Kam | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *54,55,61-64,66,68-71,73,75-97 and 99-109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54,55,61-64,66,68-71,73,77-80,99-101,104 and 107-109* is/are rejected.

7)☒ Claim(s) *75,76,81-97,102,103,105 and 106* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

1. Claims 54, 55, 61-64, 66, 68-71, 73, 75-97 and 99-109 are pending.

Applicants' amendment filed September 6, 2005 is acknowledged, and applicants' response has been fully considered. Claims 54, 61-64, 66 and 73 have been amended, claims 56-60, 65, 67, 72, 74 and 98 have been cancelled, and new claims 99-109 have been added. Therefore, claims 54, 55, 61-64, 66, 68-71, 73, 75-97 and 99-109 are examined.

### *Withdrawn-Claim Rejections - 35 USC § 112*

2. The previous rejection of claim 67, under 35 U.S.C.112, second paragraphs, is withdrawn in view of applicants' cancellation of the claim, and applicants' response at page 15 in the amendment filed September 6, 2005.

### *Withdrawn-Claim Rejections - 35 USC § 102*

3. The previous rejection of claims 54, 56-60, 75, 77-85, 87, and 91-96, under 35 U.S.C. 102(b) as being anticipated by Tomita *et al.* (U.S. Patent 5,304,633), is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at pages 11-14 in the amendment filed September 6, 2005.

4. The previous rejection of claims 54, 56-59, 65, 72, 74, 75, 77-85 and 98, under 35 U.S.C. 102(b) as being anticipated by Shimazaki *et al.* (JP-09040578), is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at pages 14-15 in the amendment filed September 6, 2005.

### *New Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 54, 55, 61-64, 66, 68-71, 73 and 99-101 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a peptide without recitation of "isolated" or "purified". As written, the claim does not explicitly indicate the hand of man. Insertion of "isolated" or "purified" in connection with a peptide is suggested. See MPEP § 2105.

***New Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 66, 104 and 107-109 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated peptide comprising SEQ ID NO:99 and wherein the peptide is SEQ ID NO:2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, and the cysteine is replaced by acetamidomethyl (Acm)-cysteine; an infant formula food comprising a peptide comprising SEQ ID NO:99 and wherein the peptide is SEQ ID NO:2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, or a method of treating infections or inflammations comprising administering to a patient the peptide of SEQ ID NO:2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, wherein the infection is urinary tract infection or colitis; or a synthetic peptide containing Acm at the Cys residue as indicated in the prior art, does not reasonably provide enablement for a peptide comprising SEQ ID NO:99, wherein SEQ ID NO:38 is excluded, where the Cys may be replaced with Cys(Acm); or an infant formula food as a foodstuff comprising the peptide, and a

method of treating inflammations or infections by administering the peptide to a patient in need thereof, but the amino acid sequence and/or the function of the peptide are not fully defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 66, 104 and 107-109 are directed to a peptide comprising SEQ ID NO:99, wherein SEQ ID NO:38 is excluded, where the Cys is replaced with Cys(Acm) (claim 66); an infant formula as a foodstuff comprising a peptide comprising SEQ ID NO:99, wherein SEQ ID NO:38 is excluded (claim 104), or a method of treating inflammations or infections comprising administering the peptide (claims 107-109). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that modified peptides from amino acid residues 20-31 of human lactoferrin, or functionally equivalent homologs or analogs of the peptides can be used for treating or preventing infections or inflammations (page 4). There are no indicia that the present application enables the full scope in view of homologs or analogs of the lactoferrin peptides and the method of treatment of infections or inflammations as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art,

the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the sequence and function of the peptides comprising SEQ ID NO:99, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

While the specification discloses specific peptides comprising SEQ ID NO:99 with a defined sequence (12 to 29 amino acid residues long) and their anti-bacterial and anti-fungal activities in vitro and in vivo (Examples 3-19 and 25-28, Figs 1-5), the specification does not describe any peptide comprising SEQ ID NO:99 with a sequence (e.g., a peptide longer than 29 amino acid residues) and function not well defined, which are encompassed by the claimed variants and the methods in association with the variants.

(3). The state of the prior art and relative skill of those in the art:

The related art (Tomita *et al.*, EP 0629347; Tomita *et al.*, U. S. Patent 5,304,633; Yamamoto *et al.*, U. S. Patent 5,565,425; Shimazaki *et al.*, JP-09040578) indicates the analogs of lactoferrin peptides with defined sequences have antimicrobial activities. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of various peptides and their functions to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass numerous peptides comprising SEQ ID NO:99, where the functions and sequences of these peptides are not defined. Therefore, it is not predictable about the effects of these peptides for the in vivo treatment of inflammations or infections.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a peptide comprising SEQ ID NO:99, wherein SEQ ID NO:38 is excluded, a foodstuff comprising the peptide, or a method of treating inflammations or infections comprising administering the peptide to a patient. The specification indicates the antimicrobial activities of various lactoferrin peptides such as specific peptides comprising SEQ ID NO:99 (Examples 3-19 and 25-28, Figs 1-5). However, the specification has not identified the functions of numerous peptides comprising SEQ ID NO:99 but with undefined sequences (e.g., peptides longer than 29 amino acid residues). Furthermore, there is no data indicating the use of these peptides in the treatment or prepared in an infant formula. Since the specification does not provide sufficient teaching regarding these numerous peptides with undefined sequences and functions, it is necessary to carry out undue experimentation to identify the functional peptides and to assess their effects in the treatment of inflammations or infections.

(6). Nature of the Invention

The scope of the claims encompasses numerous peptides comprising SEQ ID NO:99, and their use in the method of treating infections or inflammations, but the specification only shows the antimicrobial activities of specific peptides comprising SEQ ID NO:99 such as SEQ ID NO:2-5, 8, 31-37, 47, 49, 51, 63, 65, 67, 70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, it does not

demonstrate the use of numerous peptides comprising SEQ ID NO:99 with sequence and function not defined. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the sequence and function of the claimed variants are unpredictable, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify the functional peptides and to assess their effects in treating infections or inflammations.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 61-64, 77-80, 99 and 107-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 61, 63 and 64 are indefinite because claim 61 recites that the peptide is SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, however, the claim also recites the peptide further comprises GPPVSCIKR (SEQ ID NO:101) at the carboxy terminus of SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, thus, it is not clear whether the peptide is the amino acid sequence of SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, or is the amino acid sequence having SEQ ID NO:101 at the carboxy terminus of SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97. Claims 63 and 64 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

9. Claim 62 is indefinite because the claim does not further limit claim 55, which recites the specific amino acid sequence (i.e., SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97), while claim 62 recites the peptide of claim 55 further comprises the peptide of TK or SEQ ID NO:102 at the amino terminus of SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97.

*Response to Arguments*

Applicants indicate claims 61-63 have been amended to base claim 55, thus the rejection is obviated.

Applicants' response has been considered, however, the argument is not found persuasive because claim 55 recites a specific amino acid sequence identified by SEQ ID NO:70, 72, 73, 74, 80-83, 87-91, 93-95 or 97, while the dependent claim recites the peptide further comprises TK or SEQ ID NO:102 at the amino terminus, which does not further limit the scope of claim 55.

10. Claims 77-80 are indefinite because the claim do not further limit the independent claim, claim 75, which is directed to a medicinal product comprising a peptide of claim 54. The term "for treatment or prevention of infection or inflammation" is intended uses, which do not have weight in a product claim and do not limit the scope of the claim. Claims 78-80 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

11. Claim 99 is indefinite because the claim has the same scope as claim 55, both recites the peptide being SEQ ID NO: 70, 72, 73, 74, 80-83, 87-91, 93-95 or 97.

12. Claims 107-108 are indefinite because the claim lacks an essential step in the method of treating infections or inflammations. The omitted step is the outcome of the process, it is not clear what an amount of the peptide would do?

### *New Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 66 is rejected under 35 U.S.C. 102(b) as anticipated by Shimazaki *et al.* (JP-09040578, see the formal English translation mailed on 3/31/05).

Shimazaki *et al.* teach a peptide sequence of Lys-Cys*-Phe-Gln-Trp-Gln-Arg-Asn-Met-Arg-Lys-Val-Arg-Gly-Pro-Pro-Val-Ser-Cys*-Ile (SEQ ID NO:25 in the JP document; paragraph [0055]), where Cys* is cysteine that has been chemically modified with a thiol group. The reference also indicates all the protecting groups except for acetamidomethyl (Acm) were removed in the synthesis of the peptide (paragraph [0025]), and it is known Acm is a common reagent for protecting thiol group (see Art of Record). The peptide of SEQ ID NO:25 comprises SEQ ID NO:99 ($X_1$ is Gln, $X_2$ is Trp, $X_3$ is Gln, $X_4$ is Arg, $X_5$ is Asn, $X_6$ is Met, and $X_7$ is Arg), and it is not SEQ ID NO:38, which meets the criteria of claim 66.

### *Claim Objections*

14. Claims 75-76, 81-97, 102, 103, 105 and 106 are objected to as being dependent upon a rejected base claim.

***Conclusion***

15. Claims 54, 55, 61-64, 66, 68-71, 73, 77-80, 99-101, 104 and 107-109 are rejected, and claims 75-76, 81-97, 102, 103, 105 and 106 are objected to.

***Art of Record***

Greene, T. and Wuts, P. (Protective Groups in Organic Synthesis, second ed., 1991, page 293, published by John Wiley & Sons) teaches the use of acetamidomethyl (Acm) group as a protecting group for thiol, and the condition for cleavage of this protecting group.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK

November 11, 2005